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Clinical outcomes of laboratory-confirmed influenza among hospitalized patients

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Purpose

Influenza vaccination provides moderate protection against infection. Efficacy is substantially reduced when there is a mismatch between circulating influenza and vaccine serotypes.

During seasons of low vaccine effectiveness due to antigenic drift, vaccination may reduce influenza outcome severity but supporting data are limited.

More than 80% of the predominant circulating influenza A (H3N2) viruses in the United States during the 2014-2015 influenza season were antigenically different from the vaccine strain. This yielded an adjusted seasonal vaccine effectiveness of only 23%.

Objective

The objective of this study was to evaluate the association between the 2014-2015 seasonal influenza vaccine and influenza severity among hospitalized patients with laboratory-confirmed influenza infection.

Methods

The study was reviewed as exempt by the Creighton University IRB.

A retrospective chart review was performed of patients admitted to a legacy Catholic Health Initiatives (CHI) Health hospital in the Omaha-Council Bluffs metropolitan area with laboratory confirmed influenza infection between October 1, 2014 to April 30, 2015.

Adults older than 19 years of age were included if influenza was diagnosed using a rapid antigen immunoassay or multiplex polymerase chain reaction assay.

Patients were excluded if there was no documented vaccine history, administration of the seasonal influenza vaccine occurred less than 14 days prior to admission, transfer from a non-CHI hospital, received neuraminidase inhibitor therapy prior to admission, or re-hospitalization during the study interval.

The primary outcome, severe influenza, was defined by inpatient mortality, intensive care unit (ICU) admission, and/or hospital discharge to a higher level of care.

Methods (continued)

Secondary outcomes included pneumonia, pulmonary or cardiovascular complications, bacteremia, rhabdomyolysis, hypotension requiring vasopressor support, hospital length of stay, ICU length of stay (LOS), and 30-day readmission.

Patient demographic and clinical data were analyzed by influenza vaccination status.

The presence of high-risk features, classified as age > 65 years, chronic pulmonary disease, cardiovascular disease, immunodeficiency, chronic renal disease, neurological disease, nursing home or long-term care facility residency, pregnancy, alcohol abuse, and tobacco use were assessed for all patients.

Descriptive statistics were analyzed using student's t-test, chi-square test or Fisher's exact test, where appropriate.

Multivariable logistic and linear regression models evaluated the association between influenza vaccination and severe influenza, influenza complications, 30-day readmission and hospital length of stay, adjusted for covariates of gender, race, and high-risk features.

Results

Of the 156 adults hospitalized with laboratory-confirmed influenza, 111 (71%) reported receiving a non-specified 2014-2015 seasonal influenza vaccine at least 14 days before admission.

Unvaccinated patients were younger, had a lower proportion with neurologic disease, and a higher proportion with alcohol use disorder (Table 1).

After controlling for covariates, vaccination was not associated with a lower odds ratio of severe influenza (OR 0.891, 95% CI 0.335-2.369; P=0.817), pneumonia (OR 0.303, 95% CI 0.085 to 1.077; P=0.065), or hospital readmission (OR 2.481, 95% CI 0.668 to 9.225; P=0.175).

Vaccination was associated with a lower odds ratio of respiratory failure (OR 0.351, 95% CI 0.142 to 0.866; P=0.023) and a shorter hospital LOS (0.22 days; P =0.003).

Results (continued)

Table 1. Characteristics by self-reported vaccine status

Characteristic	Overall (n=156)	Vaccinated* (n=111)	Unvaccinated (n=45)	p-value
Age, median years (IQR)	74.0 (21.0)	77.0 (17.0)	64.0 (20.5)	<0.01
Female, n (%)	84 (53.8)	59 (53.2)	25 (55.6)	0.86
High-risk features, n (%)				
Age > 65 years	111 (71.2)	90 (81.1)	21 (46.7)	<0.01
COPD	69 (44.2)	55 (49.5)	14 (31.1)	0.05
Cardiac disease	70 (45.2)	43 (47.7)	17 (38.6)	0.37
Immunocompromised	22 (14.1)	15 (13.5)	7 (15.6)	0.80
CKD	69 (44.2)	47 (42.3)	22 (48.9)	0.48
Diabetes	52 (33.3)	37 (33.3)	15 (33.3)	1.00
Neurologic disease	42 (26.9)	36 (32.4)	6 (13.3)	0.02
NH or LTCF	33 (21.2)	27 (24.3)	6 (13.3)	0.19
Pregnant	0	0	0	
Smoking status				0.25
Never	65 (41.7)	43 (38.7)	22 (48.9)	
Former	75 (48.1)	58 (52.3)	17 (37.8)	
Current	16 (10.3)	10 (9.0)	6 (13.3)	
Obese, n (%)	73 (46.8)	47 (42.3)	26 (57.8)	0.11
Alcohol abuse, n (%)	8 (5.1)	3 (2.7)	5 (11.1)	0.045
Placement prior to admit, n (%)				0.68
Community-dwelling	120 (77.4)	84 (76.4)	36 (80.0)	
HHC	3 (1.9)	1 (0.9)	2 (4.4)	
ALF	12 (7.7)	10 (9.1)	2 (4.4)	
SNF/NH	18 (11.6)	13 (11.8)	5 (11.1)	
LTAC	2 (1.3)	2 (1.8)	0	
Hospice	0	0	0	
Concomitant drug therapies, n (%)				
Antibacterial	112 (71.8)	80 (72.1)	32 (71.1)	1.00
Systemic corticosteroid	67 (42.9)	51 (45.9)	16 (35.6)	0.29
NI therapy	147 (94.2)	106 (95.5)	41 (91.1)	0.28
Influenza virus subtype, n (%)				0.74
Influenza A	98 (63.2)	71 (64.5)	27 (60.0)	
Influenza B	45 (29.0)	30 (27.3)	15 (33.3)	
Both	12 (7.7)	9 (8.2)	3 (6.7)	
Time-to-antiviral therapy, median hours (IQR)	2 (3.8)	2 (3.8)	2 (3.3)	0.77

*The type of influenza vaccine was unspecified; IQR, interquartile range; COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; NH, nursing home; LTCF, long-term care facility; HHC, home health care; ALF, assisted living facility; SNF, skilled nursing facility; LTAC, long-term acute care; NI, neuraminidase inhibitor

Table 2. Disease severity, complications, and clinical outcomes associated with laboratory-confirmed influenza in hospitalized adults

Characteristic	Overall	Vaccinated*	Unvaccinated	p-value
Severe influenza, n (%)				0.38
ICU admission	21 (13.5)	14 (12.6)	7 (15.6)	
Death	1 (0.6)	1 (0.9)	0	
Discharge to a higher level of care	35 (22.4)	30 (27.0)	5 (11.1)	
Respiratory complications, n (%)				
Respiratory failure	58 (37.2)	38 (34.2)	20 (44.4)	0.27
Pneumonia	42 (26.9)	28 (25.2)	14 (31.1)	0.55
Exacerbation of chronic lung disease	40 (25.6)	33 (29.7)	7 (15.6)	0.07
Cardiovascular complications, n (%)				
Hypotension	9 (5.8)	5 (4.5)	4 (8.9)	0.28
Decompensated HF	13 (8.3)	9 (8.1)	4 (8.9)	1.00
MI	3 (1.9)	2 (1.8)	1 (2.2)	1.00
CVA/TIA	1 (0.6)	1 (0.9)	0	1.00
Hospital LOS, median days (IQR)	7.0 (6.3)	7.0 (5.0)	7.0 (9.0)	0.69
ICU LOS, median days (IQR)	4.0 (4.0)	4.0 (5.0)	3.0 (5.0)	0.81
30-day readmission	21 (13.5)	17 (15.5)	4 (8.9)	0.44

*The type of influenza vaccine was unspecified; ICU, intensive care unit; HF, heart failure; MI, myocardial infarction; CVA, cerebrovascular accident; TIA, transient ischemic attack; LOS, length of stay; IQR, interquartile range

Conclusions

Use of the 2014-2015 seasonal influenza vaccine was not associated with a lower odds of severe influenza in this cohort but patients who reported receiving the vaccine had a lower risk of respiratory failure and a shorter hospital LOS.

The observational study design may introduce confounding variables which limit the ability to establish a cause-effect relationship.

The association of seasonal influenza vaccine on disease severity remains uncertain. Large randomized controlled trials would be optimal to determine the true effect of the influenza vaccination on clinical outcomes, particularly in seasons with a high mismatch between vaccine and circulating viruses. However, such a design would raise ethical concerns given that influenza vaccination is the standard of practice for all individuals 6 months of age and older in the United States.

References

1. Fry AM, Kim IK, Reed C, et al. Modeling the effect of different vaccine effectiveness estimates on the number of vaccine-prevented influenza-associated hospitalizations in older adults. *Clin Infect Dis.* 2014;59(3):406-9.
2. Centers for Disease Control and Prevention. Influenza (Flu) Information for Specific Groups. http://www.cdc.gov/flu/groups.htm. Accessed July 18, 2015.
3. Centers for Disease Control and Prevention. CDC Presents Updated Estimates of Flu Vaccine Effectiveness for the 2015-2015 Season. http://www.cdc.gov/flu/news/updated-vaccine-effectiveness-2014-15.htm. Accessed July 18, 2015.
4. Arriola CS, Anderson EJ, Baumbach J, et al. Does influenza vaccination modify influenza severity? Data on older adults hospitalized with influenza during the 2012-2013 season in the united states. *J Infect Dis.* 2012; jiv200v2-jiv200.

Disclosures

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